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FALL IN PLASMA CONTENT OF FREE FATTY ACIDS ASSOCIATED WITH SIGHT OF FOOD*

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A RELATION between blood glucose and free fatty acids in the blood has been known since Dole's¹ paper was published in 1956. In the postabsorptive state, when readily available carbohydrate stores have been exhausted, free fatty acids are mobilized from fat stores by hydrolysis of triglycerides under the influence of the sympathetic nervous system, by the mediation of both epinephrine and norepinephrine. This increased mobilization is reflected in relatively high levels of free fatty acids in plasma. In the immediate postprandial state, with elevated blood glucose levels and easily available carbohydrate, mobilization of free fatty acids decreases and relatively low levels are found in the plasma. In general, there is a reciprocal relation between blood glucose and plasma free fatty acids (Fig. 1).

Some informal experiments in our laboratory suggested that when a subject ingests food, free fatty acids might fall before blood glucose rose — in fact, in anticipation of food ingestion. Reductions in free fatty acids were noted in response to the ingestion of noncaloric ginger ale, black coffee and water. These experiments suggested that an anticipatory fall in free fatty acids mediated by the central nervous system might occur even when a carbohydrate load was not ingested at all. The following experiments were designed to test the effect of looking at and tasting food on plasma free fatty acids in healthy persons.

METHODS

Subjects for these experiments were medical-stu-

dent volunteers of normal weight. They were studied in 3 series of experiments. Generally, after a five-hour fast, each subject came to the laboratory, where a No. 20 indwelling needle was placed in one of his antecubital veins. During a control period of varying duration (Table 1) samples of blood were taken. At the conclusion of the control period, subjects were presented with appetizing food and were required to look at it for one minute. After this, another sample of blood was obtained. Subjects then took a very small bite of food; an additional blood sample was obtained one minute after this bite. The subject then finished the food. Rare roast beef or a roast-beef sandwich was used as the test food. Samples were analyzed for free fatty acids by the method of Dole,¹ and for glucose by the Somogyi-Nelson method. All samples were transferred to heparinized tubes immediately; plasma was removed and frozen within thirty minutes. Subjects were asked not to smoke for four hours before the experiment and to refrain from strenuous physical exertion during this time. They were fully informed about the nature of the experiments, all of which were performed singly, in the same room, by the same investigators.

RESULTS

First Series

Figure 2 shows an example of the effect of the sight of food on free fatty acids. In 18 of 24 experiments, 1 of the values after was lower than either of the 2 values before food presentation. Subjects usually volunteered that the sight of the sandwich made them extremely hungry and that epigastric tightness and salivation were associated with the

TABLE 1. *Methods.*

SERIES	NO. OF SUBJECTS	NO. OF SESSIONS/ SUBJECT	TIME OF DAY	TIME BETWEEN CONTROL SAMPLES	NO. OF CONTROL SAMPLES
				min.	
1st	12	2	Noon	20	3
2d	3	4	Evening	5	3
3d	3	6	Noon	5	Variable

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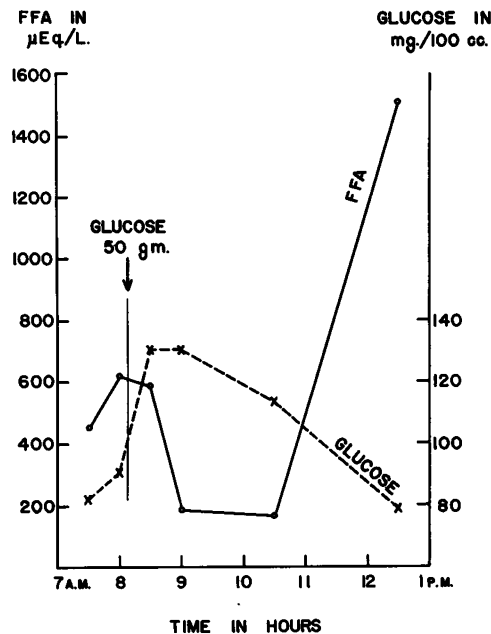


FIGURE 1. Relation between Blood Glucose and Free Fatty Acids (Adapted from Dole¹).

one-minute period of looking at the sandwich. There was no pattern to the occurrence of this phenomenon; some subjects exhibited it in both sessions, some in the first but not in the second, some in the second but not in the first, and some not at all. Blood glucose showed no significant changes; values remained at normal fasting levels throughout.

Second Series

A second series of experiments was carried out with certain modifications. To minimize clotting problems with the indwelling needle, the period between the control samples was shortened from twenty to five minutes. In this series the meal was presented at the time of the subject's usual evening meal, and blood glucose levels were determined in the first sample only, to provide evidence that the level was not elevated at the time the experiment

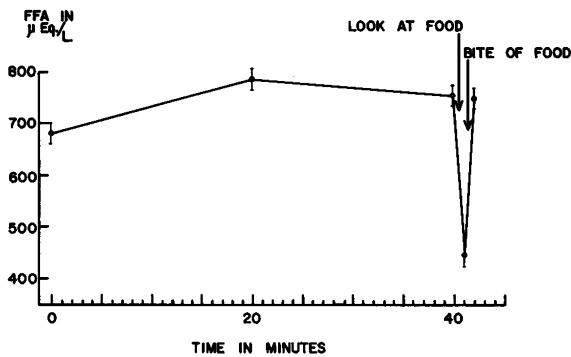


FIGURE 2. Effect of the Sight of Food on Free Fatty Acids.

began. Three subjects participated in 4 experimental sessions each. All blood glucose determinations were in the normal fasting range during these experiments. Free fatty acids fell after the presentation of food in 9 of the 12 experiments.

Third Series

The frequency of fall in fatty acids after food presentation attained statistical significance in the first series (chi square equal to 5.04, and p less than 0.05), but not in the second (chi square equal to 2.08, and p less than 0.20). Therefore, the possibility that the findings were the result of random variation in levels of free fatty acids had to be seriously entertained. The level is known to be extremely labile and is sensitive to pain, fear and anxiety.² Variation in base-line levels occurred regularly. It was difficult to be certain that the fall after presentation of food might not be initiated by other cues arising from the environment, particularly when both the subject and the operator knew when the food was to be presented. Furthermore, failure to observe a fall in free fatty acids was often associated with mechanical difficulty with the indwelling needle. Therefore, a third series of experiments was designed to minimize the possible effects of these factors.

Three healthy volunteers with good veins were selected. A double-blind, randomized schedule was devised so that neither the subject nor the operator knew when the sandwich would be presented. It might be presented after either the second, the third, the fourth or the fifth control sample. As a further control, 1 series of experiments was carried out in which only an empty plate was presented after the fourth control sample, and another series was carried out in which nothing whatever was presented.

The results are shown in Figures 3 and 4. The fall in free fatty acids occurred whether the food was presented after the second, the third, the fourth or the fifth control sample. These 4 situations were randomly presented. The fifth session for each subject was the empty plate (Fig. 4A), and the sixth was the control (Fig. 4B). In Figure 5 the comparison between the effect of the sandwich, the empty plate and the presentation of nothing at all is shown for a single subject.

Because of base-line variability in free fatty acids we did not attempt to compare mean values, but relied on a cumulative chi-square test. The hypothesis was set up that if food presentation had no effect on free fatty acids, the time of the lowest value in any series should not be affected by whether or not the sample was obtained before or after food presentation. Since there were different numbers of control samples the statistical analysis was carried out by determination of the expected distribution of lowest values for each series of 3 experiments based on the null hypothesis of an

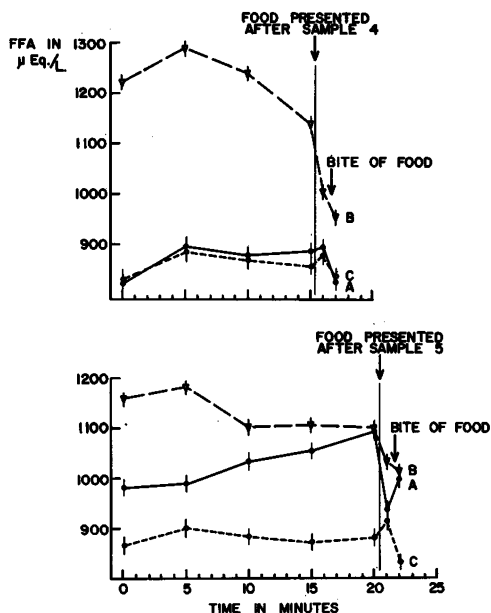


FIGURE 3. Fall in Free Fatty Acids with Presentation of Food after Sample 4 (A) and Sample 5 (B).

equal chance that the lowest value might occur in any sample. When the observed and the expected findings were compared for the three series of experiments, the chi-square value was calculated to be 11.612, with 1 degree of freedom, p being less than 0.001. Viewed most simply, the lowest value for

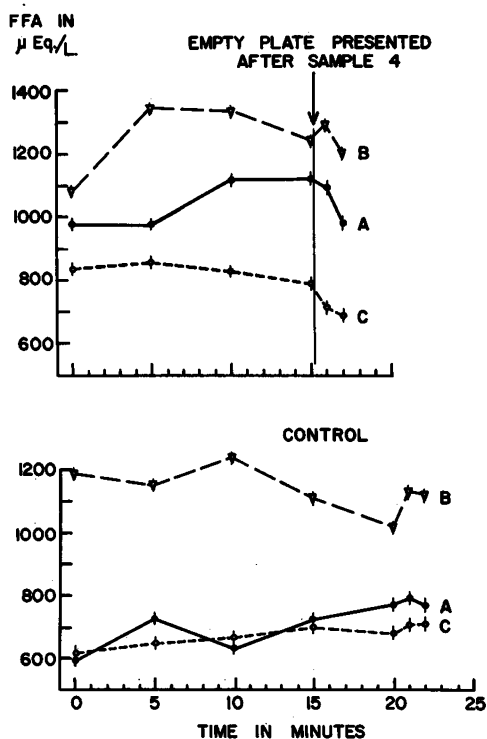


FIGURE 4. Effect of Presentation of an Empty Plate after Sample 4 (A) as Compared with Control Sample (B).

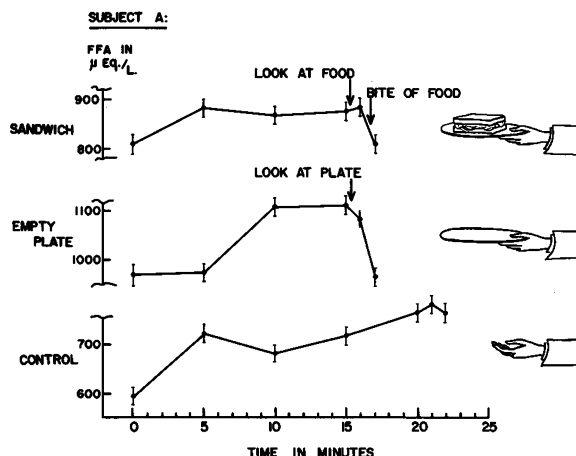


FIGURE 5. Effect of a Sandwich, an Empty Plate and Presentation of Nothing at All on a Single Subject.

free fatty acids occurred in 10 of 24 samples after food presentation, and in only 2 of 42 samples taken before presentation. The finding is consistent with the hypothesis that free fatty acids fell in association with the sight or taste of food.

DISCUSSION

The half-life of free fatty acids in plasma is approximately two minutes because of the rapid metabolism of these fat fractions.³ When mobilization of free fatty acids is slowed down, a fall in level of circulating free fatty acids may be observed within one minute. Apparently, the sight or taste of food may be a sufficient stimulus to some hungry people to cause their mobilization of free fatty acids to slow down "in anticipation" of a carbohydrate load. Usually, after the initial anticipatory drop, levels of free fatty acids rise again as the mobilization of fat is resumed. Our data do not exclude increased utilization as a cause of the reduction. Decreased mobilization as the explanation for this phenomenon is therefore hypothetical. It is of interest that subjects often volunteered that the sight of the sandwich produced acute sensations of hunger. Subjects noted increased salivation and a tight sensation in the epigastrium while looking at the sandwich. Attempts to correlate degree of hunger with the promptness and magnitude of the fall in free fatty acids have not been pursued in detail.

It is possible that, under ordinary circumstances, this drop in free fatty acids is a part of a bodily reaction comparable to events such as increased salivation and increased gastric tone and secretion. Generally, this transitory state immediately before eating may be looked upon as resulting from a decrease in sympathetic tone and an increase in vagal tone. Appetite-depressing drugs are sympathomimetic agents. Therefore, they act to decrease gastric tone and secretion and to mobilize free fatty acids. It is thus likely that commonly used appetite-

depressing drugs would prevent the fall in free fatty acids that we have observed. Glucagon, which we have used as an appetite depressant,⁴ also reduces gastric tone and secretion, and tends to promote mobilization of free fatty acids.⁵ Studies are currently in progress to delineate the relation between fatty acid mobilization and appetite-depressing drugs.

SUMMARY

The results reported demonstrate that, in a small sample of healthy males, a fall in free fatty acid concentration in the plasma took place within one minute after the presentation of food. A double-blind randomized schedule of food presentation

permitted isolation of the sandwich, and in 1 test, of the empty plate, as the inciting factor. Since neither the subject nor the operator knew when the sandwich was to be presented, the interference of other cues was minimized.

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SPECIAL ARTICLE

ORIGINS, TREATMENT AND DESTINY OF SKID-ROW ALCOHOLIC MEN*

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THIS paper reports a ten-year-follow-up study of a group of indigent alcoholic men. In 1950 we established a work-oriented halfway-house program for their rehabilitation at the Boston Long Island Hospital.¹ In 1956 we evaluated 101 patients who had volunteered for this program four years previously.² In 1962 we re-evaluated this treatment group. For comparison, we made an extensive record search not only of these 101 patients but of an additional 108 skid-row alcoholics who entered the Hospital in 1952 but who, for one reason or another, never applied for the halfway-house treatment program. This record search consisted of gathering data from probation records, hospital records from Boston City and Massachusetts General hospitals, death records and State Hospital records. In addition, we collected the social-service indexes not only of these 101 treatment and 108 comparison patients but also of their parents, wives and children, if any. Each social-service index recorded the

patient's and his family's contacts with various social service agencies, such as public welfare, society for the prevention of cruelty to children and division of child guardianship and various treatment agencies. These data enabled us to obtain a 2-generation and, in some cases, a 3-generation, picture of these skid-row alcoholic men.

In this paper we shall first briefly set forth the program and then describe the background of these two groups, with particular attention to similarities and differences in their origins, marriages, work adjustment and police records. We shall then present in detail the outcome of the treatment group from 1952 to 1962. Finally, we shall discuss the treatment program, offering recommendations for broader and more preventive treatment programs.

THE PROGRAM

For many years Boston Long Island Hospital has served the needs of the city's indigent and homeless. In addition to serving patients with chronic illnesses such as arthritis and cardiac disturbances, it is one of the few hospitals to offer institutional care for the skid-row man. The Hospital has maintained a 300-bed dormitory to which the alcoholic man may come, withdraw from alcohol, stay as long as he wishes and leave at any time. In 1950 we converted one ward of the dormitory into a "halfway house." Men who volunteered for the halfway-house program worked during the day in the city, spent nights in the ward and used weekends to

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